

What is claimed is:

1. A compound having the structure:



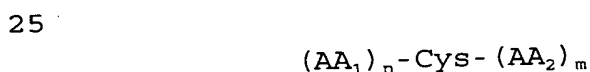
wherein $n = 0, 1, 2, 3, 4$ or 5 and $m = 0, 1, 2, 3, 4$ or 5 ,
provided the sum of $(n + m)$ is greater than or equal to
two and less than or equal to five,

10 if $n = 1$, $(AA_1)_n = \text{Ala-}$,
 if $n = 2$, $(AA_1)_n = \text{Gln-Ala-}$,
 if $n \geq 3$, $(AA_1)_n = (\text{Xaa})_p\text{-Gln-Ala-}$,

and Xaa = any amino acid and

 wherein if $n = 3$, $p = 1$,
15 if $n = 4$, $p = 2$,
 if $n = 5$, $p = 3$,
 if $m = 1$, $(AA_2)_m = \text{-Arg}$,
 if $m = 2$, $(AA_2)_m = \text{-Arg-Gly}$,
 if $m \geq 3$, $(AA_2)_m = \text{-Arg-Gly-(Xaa)}_q$,
20 wherein if $m = 3$, $q = 1$,
 if $m = 4$, $q = 2$,
 if $m = 5$, $q = 3$.

2. A compound having the structure:



wherein $n = 0, 1, 2$ or 3 and $m = 0, 1, 2$ or 3 ,
provided the sum of $(n + m)$ is greater than or equal to
two and less than or equal to five,

30 if $n = 1$, $(AA_1)_n = \text{Ala-}$,
 if $n = 2$, $(AA_1)_n = \text{Gln-Ala-}$,
 if $n = 3$, $(AA_1)_n = (\text{Xaa})_p\text{-Gln-Ala-}$,

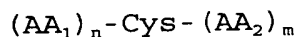
and Xaa = any amino acid and

35 wherein if $n = 3$, $p = 1$,

if $m = 1$, $(AA_2)_m = -\text{Arg}$,
if $m = 2$, $(AA_2)_m = -\text{Arg-Gly}$,
if $m = 3$, $(AA_2)_m = -\text{Arg-Gly-(Xaa)}_q$,
wherein if $m = 3$, $q = 1$.

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3. A compound having the structure:



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wherein $n = 2$ or 3 and $m = 0, 1, 2$ or 3 ,
provided the sum of $(n + m)$ is greater than or equal to
two and less than or equal to five,

if $n = 2$, $(AA_1)_n = \text{Gln-Ala-}$,

if $n = 3$, $(AA_1)_n = (\text{Xaa})_p\text{-Gln-Ala-}$,

15

and $\text{Xaa} = \text{any amino acid}$ and

wherein if $n = 3$, $p = 1$,

if $m = 1$, $(AA_2)_m = -\text{Arg}$,

if $m = 2$, $(AA_2)_m = -\text{Arg-Gly}$,

if $m = 3$, $(AA_2)_m = -\text{Arg-Gly-(Xaa)}_q$,

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wherein if $m = 3$, $q = 1$.

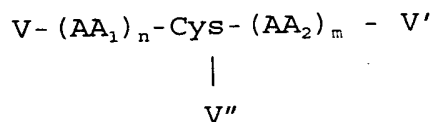
4. The compound of claim 1, wherein the compound is Ile-Gln-Ala-Cys-Arg-Gly (Seq. I.D. No. 1).

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5. The compound of claim 1, wherein the compound is Gln-Ala-Cys-Arg-Gly (Seq. I.D. No. 3).

6. A compound having the structure:

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wherein $n = 0, 1, 2, 3, 4$ or 5 and $m = 0, 1, 2, 3, 4$ or 5 ,

provided the sum of $(n + m)$ is greater than or equal to

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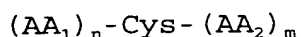
two and less than or equal to five,

- if $n = 1$, $(AA_1)_n = \text{Ala-}$,
if $n = 2$, $(AA_1)_n = \text{Gln-Ala-}$,
if $n \geq 3$, $(AA_1)_n = (\text{Xaa})_p\text{-Gln-Ala-}$,
and Xaa = any amino acid and
5 wherein if $n = 3$, $p = 1$,
if $n = 4$, $p = 2$,
if $n = 5$, $p = 3$,
if $m = 1$, $(AA_2)_m = \text{-Arg}$,
if $m = 2$, $(AA_2)_m = \text{-Arg-Gly}$,
10 if $m \geq 3$, $(AA_2)_m = \text{-Arg-Gly-(Xaa)}_q$,
wherein if $m = 3$, $q = 1$,
if $m = 4$, $q = 2$,
if $m = 5$, $q = 3$,
wherein each V, V' or V'' is independently an agent
15 capable of specifically directing the compound to a cell.
7. The compound of claim 6, wherein V, V' or V'' is a
polypeptide comprising at least a portion of an
Antennepedia polypeptide.
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8. The compound of claim 7, wherein V, V' or V'' is at least
a portion of a polypeptide comprising the sequence NPyS-
Arg-Gln-Ile-Lys-Ile-Trp-Phe-Gln-Asn-Arg-Arg-Met-Lys-Trp-
Lys-Lys-(Seq. I.D. No. 9).
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9. The compound of claim 8, wherein the compound is NPyS-
Arg-Gln-Ile-Lys-Ile-Trp-Phe-Gln-Asn-Arg-Arg-Met-Lys-Trp-
Lys-Lys-Ile-Gln-Ala-Cys-Arg-Gly (Seq. I.D. No. 10).
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10. The compound of claim 8, wherein the compound is
NPyS-Arg-Gln-Ile-Lys-Ile-Trp-Phe-Gln-Asn-Arg-Arg-
Met-Lys-Trp-Lys-Lys-Gln-Ala-Cys-Arg-Gly (Seq. I.D.
No. 11).
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11. The compound of claim 6, wherein each V, V' or V''

is independently an antibody, an adjuvant or a cell-specific ligand.

12. The compound of claim 6, wherein the cell is a neuronal cell, a cardiac cell or a liver cell.

13. A peptidomimetic compound having the biological activity of the structure:



wherein $n = 0, 1, 2, 3, 4$ or 5 and $m = 0, 1, 2, 3, 4$ or 5 , provided the sum of $(n + m)$ is greater than or equal to two and less than or equal to five,

if $n = 1$, $(AA_1)_n = \text{Ala-}$,

if $n = 2$, $(AA_1)_n = \text{Gln-Ala-}$,

if $n \geq 3$, $(AA_1)_n = (\text{Xaa})_p\text{-Gln-Ala-}$,

and Xaa = any amino acid and

wherein if $n = 3$, $p = 1$,

if $n = 4$, $p = 2$,

if $n = 5$, $p = 3$,

if $m = 1$, $(AA_2)_m = \text{-Arg}$,

if $m = 2$, $(AA_2)_m = \text{-Arg-Gly}$,

if $m \geq 3$, $(AA_2)_m = \text{-Arg-Gly-(Xaa)}_q$,

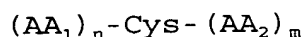
wherein if $m = 3$, $q = 1$,

if $m = 4$, $q = 2$,

if $m = 5$, $q = 3$,

having a bond, a peptide backbone or an amino acid component replaced with a suitable mimic.

14. A pharmaceutical composition comprising an amount of a compound having the structure:



wherein $n = 0, 1, 2, 3, 4$ or 5 and $m = 0, 1, 2, 3, 4$ or 5 ,
provided the sum of $(n + m)$ is greater than or
equal to two and less than or equal to five,

if $n = 1$, $(AA_1)_n = \text{Ala-}$,

5 if $n = 2$, $(AA_1)_n = \text{Gln-Ala-}$,

if $n \geq 3$, $(AA_1)_n = (\text{Xaa})_p\text{-Gln-Ala-}$,

and Xaa = any amino acid and

wherein if $n = 3$, $p = 1$,

if $n = 4$, $p = 2$,

10 if $n = 5$, $p = 3$,

if $m = 1$, $(AA_2)_m = \text{-Arg}$,

if $m = 2$, $(AA_2)_m = \text{-Arg-Gly}$,

if $m \geq 3$, $(AA_2)_m = \text{-Arg-Gly-(Xaa)}_q$,

wherein if $m = 3$, $q = 1$,

15 if $m = 4$, $q = 2$,

if $m = 5$, $q = 3$,

effective to inhibit the death of a cell and a
pharmaceutically acceptable carrier thereof.

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15. The pharmaceutical composition of claim 14, wherein
the compound is Ile-Gln-Ala-Cys-Arg-Gly (Seq. I.D.
No. 1).

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16. The pharmaceutical composition of claim 14, wherein
the compound is Gln-Ala-Cys-Arg-Gly (Seq. I.D. No.
3).

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17. The pharmaceutical composition of claim 14, wherein
the cell is a neuronal cell, a cardiac cell or a
hepatic cell.

18. The pharmaceutical composition of claim 14, wherein
the carrier comprises a diluent.

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19. The pharmaceutical composition of claim 14, wherein the carrier comprises an appropriate adjuvant, a herpes virus, a liposome, a microencapsule, a neuronal cell receptor ligand, a neuronal-specific virus, a polymer encapsulated cell or a retroviral vector.

20. The pharmaceutical composition of claim 14, wherein the pharmaceutically acceptable carrier is an aerosol, intravenous, oral or topical carrier.

21. A method of inhibiting death of a cell which comprises contacting the cell with an amount of a compound having the structure:



wherein $n = 0, 1, 2, 3, 4$ or 5 and $m = 0, 1, 2, 3, 4$ or 5 , provided the sum of $(n + m)$ is greater than or equal to two and less than or equal to five,

if $n = 1$, $(AA_1)_n = \text{Ala-}$,

if $n = 2$, $(AA_1)_n = \text{Gln-Ala-}$,

if $n \geq 3$, $(AA_1)_n = (\text{Xaa})_p\text{-Gln-Ala-}$,

and $\text{Xaa} = \text{any amino acid and}$

wherein if $n = 3$, $p = 1$,

if $n = 4$, $p = 2$,

if $n = 5$, $p = 3$,

if $m = 1$, $(AA_2)_m = \text{-Arg}$,

if $m = 2$, $(AA_2)_m = \text{-Arg-Gly}$,

if $m \geq 3$, $(AA_2)_m = \text{-Arg-Gly-(Xaa)}_q$,

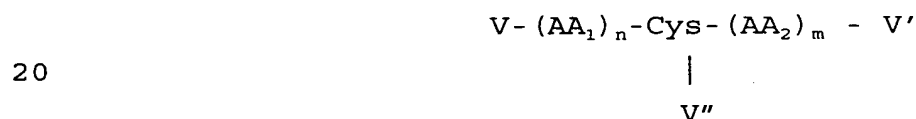
wherein if $m = 3$, $q = 1$,

if $m = 4$, $q = 2$,

if $m = 5$, $q = 3$,

effective to inhibit death of the cell.

22. The method of claim 21, wherein the compound is Ile-Gln-Ala-Cys-Arg-Gly (Seq. I.D. No. 1).
23. The method of claim 21, wherein the compound is Gln-Ala-Cys-Arg-Gly (Seq. I.D. No. 3).
24. The method of claim 21, wherein the cell is in a subject.
25. The method of claim 21, wherein the subject is a human.
26. The method of claim 21, wherein the cell is a neuronal cell, a cardiac cell or a hepatic cell.
27. A method of inhibiting death of a cell using a compound having the structure:



- wherein $n = 0, 1, 2, 3, 4$ or 5 and $m = 0, 1, 2, 3, 4$ or 5 , provided the sum of $(n + m)$ is greater than or equal to two and less than or equal to five,
- if $n = 1$, $(AA_1)_n = \text{Ala-}$,
- if $n = 2$, $(AA_1)_n = \text{Gln-Ala-}$,
- if $n \geq 3$, $(AA_1)_n = (\text{Xaa})_p\text{-Gln-Ala-}$,
- and Xaa = any amino acid and
- wherein if $n = 3$, $p = 1$,
- if $n = 4$, $p = 2$,
- if $n = 5$, $p = 3$,
- if $m = 1$, $(AA_2)_m = \text{-Arg}$,
- if $m = 2$, $(AA_2)_m = \text{-Arg-Gly}$,
- if $m \geq 3$, $(AA_2)_m = \text{-Arg-Gly-(Xaa)}_q$,
- wherein if $m = 3$, $q = 1$,

if $m = 4$, $q = 2$,

if $m = 5$, $q = 3$,

wherein V, V' or V'' is independently an agent capable of specifically directing the compound to a cell which comprises contacting the cell with an amount of the compound effective to inhibit cell death.

28. The method of claim 27, wherein V, V' or V'' is a polypeptide comprising at least a portion of an Antennepedia polypeptide.
29. The method of claim 27, wherein V, V' or V'' is a polypeptide comprising the sequence NPyS-Arg-Gln-Ile-Lys-Ile-Trp-Phe-Gln-Asn-Arg-Arg-Met-Lys-Trp-Lys-Lys-(Seq. I.D. No. 9).
30. The method of claim 27, wherein the compound is NPyS-Arg-Gln-Ile-Lys-Ile-Trp-Phe-Gln-Asn-Arg-Arg-Met-Lys-Trp-Lys-Lys-Ile-Gln-Ala-Cys-Arg-Gly (Seq. I.D. No. 10).
31. The method of claim 27, wherein the compound is NPyS-Arg-Gln-Ile-Lys-Ile-Trp-Phe-Gln-Asn-Arg-Arg-Met-Lys-Trp-Lys-Lys-Gln-Ala-Cys-Arg-Gly (Seq. I.D. No. 11).
32. The method of claim 27, wherein V, V' or V'' is an antibody, an adjuvant or a cell-specific ligand.
33. The method of claim 27, wherein the cell is in a subject.
34. The method of claim 27, wherein the subject is a human.

35. The method of claim 27, wherein the cell is a neuronal cell, a cardiac cell or a hepatic cell.
- 5 36. A method for alleviating symptoms of a neurodegenerative disorder in a subject which comprises administering to the subject either the compound of claim 1 or 6, the compound being present in an amount effective to inhibit neuronal cell death and thus alleviate the symptoms of the neurodegenerative disorder in the subject.
- 10 37. The method of claim 36, wherein the neurodegenerative disorder is associated with aging, Alzheimer's disease, dentatorubral and pallidolysian atrophy, Huntington's disease, Machado-Joseph disease, multiple sclerosis, muscular dystrophy, Parkinson's disease, senility, spinocerebellar ataxia type I, spinobulbar muscular atrophy, stroke, trauma.
- 15 38. The method of claim 36, wherein the subject is a mammal.
- 20 39. The method of claim 38, wherein the mammal is a human.
- 25 40. The method of claim 36, wherein the administration comprises aerosol delivery; intralesional, intraperitoneal, intramuscular or intravenous injection; infusion; liposome-mediated delivery; anal, nasal, oral, ocular, otic or topical delivery of the pharmaceutical composition.
- 30 41. A method for alleviating symptoms of a cardiovascular disorder in a subject which
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5 comprises administering to subject either the compound of the claim 1 or 6, the compound being present in an amount effective to inhibit cardiac cell death and thus alleviate the symptoms of the cardiovascular disorder in the subject.

10 42. A method of alleviating symptoms of a liver disorder in a subject which comprises administering to the subject either the compound of claim 1 or 6, the compound being present in an amount effective to inhibit liver cell death and thus, alleviate the symptoms of the liver disorder in the subject.

15 43. A method of inhibiting a biological activity associated with ICE in a cell which comprises contacting the cell with an effective amount of the compound of claim 1.

20 44. A method of identifying a peptide compound as an enzyme inhibitor which comprises preparing suitable peptide fragments chosen from an active site of an enzyme, assaying the fragments and identifying the fragments which are enzyme inhibitors.

25 45. A compound obtained by the method of claim 44.

30 46. A method of inhibiting the activity of an enzyme on a substrate which comprises contacting the enzyme with a peptide fragment or a peptidomimetic fragment from an active site of the enzyme under conditions that the fragment is capable of binding to the substrate of the enzyme and thus inhibiting the activity of the enzyme on the substrate.

35 47. A method of inhibiting the activity of an enzyme on

5 a substrate in a cell which comprises contacting the enzyme with a peptide fragment or a peptidomimetic fragment from an active site of the enzyme under conditions that the fragment is capable of binding to the substrate of the enzyme and thus inhibiting the activity of the enzyme on the substrate.